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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/719,540	11/20/2003	Ron L. Hale	00063.01R	3439
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SWANSON & BRATSCUN, L.L.C 8210 SOUTHPARK TERRACE LITTLETON, CO 80120			EXAMINER ALSTRUM ACEVEDO, JAMES HENRY	
			ART UNIT 1616	PAPER NUMBER
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/719,540	Applicant(s) HALE ET AL.	
	Examiner James H. Alstrum-Acevedo	Art Unit 1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 15 October 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1 and 5-24 is/are pending in the application.
- 4a) Of the above claim(s) 21-23 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1, 5-20 and 24 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Claims 1 and 5-24 are pending. Applicants have cancelled claims 2-4. Applicants have amended claims 1 and 5-20. Claims 21-23 were withdrawn from consideration because these were drawn to non-elected subject matter. **Claims 1, 5-20, and 24 are under consideration** in the instant office action. Receipt and consideration of Applicants' amended claims and remarks/arguments, submitted on August 15, 2007 are acknowledged.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on October 15, 2007 has been entered.

Election/Restrictions

Applicant's election without traverse of Group I in the reply filed on November 30, 2006 is acknowledged. The requirement is deemed proper and is therefore made FINAL.

Moot Rejections/objections

All rejections and/or objections of claims 2-4 cited in the previous office action mailed on February 15, 2007 **are moot**, because said claims have been cancelled.

Specification

The objection to the specification for the incorporation of essential material in the specification by reference to an unpublished U.S. application, foreign application or patent is withdrawn (see advisory action mailed 8/29/07).

Claim Rejections - 35 USC § 102

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

The rejection of claims 1 and 10-15 under 35 U.S.C. 102(e) as being anticipated by Dehaven et al. (WO 02/060870; IDS) is withdrawn due to Applicants' amendments requiring that the method of treatment be limited to the treatment of headache.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Applicant Claims
2. Determining the scope and contents of the prior art.

3. Ascertaining the differences between the prior art and the claims at issue, and resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

The rejection of claims 1-9 and 24 under 35 U.S.C. 103(a) as being unpatentable over Burns et al. (U.S. Patent No. 5,284,133) **is maintained** for the reasons of record set forth on pages 7-10 of the office action mailed on June 2, 2006.

Response to Arguments

Applicant's arguments filed August 15, 2007 have been fully considered but they are not persuasive. Applicants' traversal arguments of the above rejection under 35 U.S.C. §103(a) are: (1) it was inappropriate to read the teachings of Burns to mean that loxapine hydrochloride was a known headache analgesic; (2) the identification of loxapine hydrochloride as a headache analgesic was allegedly only possible by impermissible hindsight reconstruction of Applicants' specification; and (3) Burns brief list of examples of migraine analgesics does not include

loxapine hydrochloride, which allegedly implies that loxapine hydrochloride was not considered a migraine analgesic.

The Examiner respectfully disagrees with Applicants traversal arguments. Regarding (1), this argument was previously rebutted in the office action mailed on 2/15/07 and the Office's position is unchanged. In response to applicant's argument (2) that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971). Regarding (3), Burns list is clearly not intended as being an exhaustive list of every known migraine analgesic and the mere fact that Burns chose not to explicitly cite loxapine hydrochloride as a migraine analgesic does not lead one to conclude that loxapine hydrochloride is not a migraine analgesic., nor would the teachings of burns in column 7, lines 25-27 discourage an ordinary skilled artisan from using loxapine hydrochloride to treat a migraine. Thus the instant rejection is considered to remain proper.

The rejection of claims 10-15 under 35 U.S.C. 103(a) as being unpatentable over Burns et al. (U.S. Patent No. 5,284,133) as applied to claims 1-9 and 24 above, and further in view of Drug Information Handbook, 2nd edition (Lexi-Comp, Inc.: Cleveland, 1994-1995, pp 554-555) ("DIH") **is maintained** for the reasons of record set forth on pages 11-12 of the office action mailed on June 2, 2006.

Response to Arguments

Applicant's arguments filed August 15, 2007 have been fully considered but they are not persuasive. Applicants' traversal arguments of the above rejection under 35 U.S.C. §103(a) are: (1) Burns allegedly does not teach loxapine hydrochloride for the treatment of headache and (2) the dosages taught by the DIH would allegedly provide no suggestion of suitable dosages for the inhalation administration of loxapine hydrochloride to treat headache.

The Examiner respectfully disagrees with Applicants' traversal arguments. Argument (1) has already been addressed above and its rebuttal is herein incorporated by reference. Regarding (2), it would have been apparent to a skilled artisan that the dosages required for inhalation administration would be lower than those for oral administration (DIH), because via inhalation administration the disadvantage of first-pass metabolism of the administered drug by the liver and kidneys is avoided (Burns). Therefore a lower amount of drug would be needed if administered by inhalation. The skilled artisan would utilize the teachings of the DIH regarding the oral doses as a maximum starting point from which to undertake routine optimization of dosage amounts as practiced in the art and it would have been well within the skill of the ordinary skilled artisan to ascertain what dosage amount is suitable for effective analgesia of headaches and migraines. Regarding Applicants' specification paragraphs 24-25, these paragraphs are not found persuasive in rebutting the prima facie case of obviousness. The instant rejection remains proper.

The rejection of claims 16-17 and 19-20 under 35 U.S.C. 103(a) as being unpatentable over Burns et al. (U.S. Patent No. 5,284,133) as applied above to claims 1-15 and 24 and further in view of Nguyen et al. (U.S. Patent No. 7,040,314) **is maintained** for the reasons of record set forth on pages 12-15 of the office action mailed on June 2, 2006.

The rejection of claims 16-18 under 35 U.S.C. 103(a) as being unpatentable over Burns et al. (U.S. Patent No. 5,284,133) as applied to claims 1-9 and 24 above, and further in view of Rabinowitz et al. (US 2004/0009128) **is maintained** for the reasons of record set forth on pages 15-17 of the office action mailed on June 2, 2006.

Response to Arguments

Applicant's arguments filed August 15, 2007 have been fully considered but they are not persuasive. Applicants' traversal of the above rejections based on a combination of Burns with either Nguyen or Rabinowitz under 35 U.S.C. §103(a) are: (1) Burns allegedly fails to disclose the administration of loxapine hydrochloride to treat headache; and (2) the secondary references Nguyen or Rabinowitz do not allegedly cure these deficiencies.

The Examiner respectfully disagrees. Argument (1) has already been addressed above and its rebuttal is herein incorporated by reference. Argument (2) is not material, because (1) has been clearly and unambiguously rebutted. Therefore, the aforementioned rejections under 35 U.S.C. §103(a) remain proper.

Claims 1 and 10-15 are rejected 35 U.S.C. 103(a) as being unpatentable over Dehaven et al. (WO 02/060870; IDS).

Applicant Claims

Applicants claim a method of treating headache comprising administering to a subject in need of headache relief an effective amount of loxapine or pharmaceutically acceptable salts or prodrugs thereof.

Determination of the Scope and Content of the Prior Art (MPEP §2141.01)

The teachings of Dehaven were originally set forth on page 6 of the office action mailed on June 2, 2006. These teachings are restated herein for Applicants' convenience. Dehaven teaches in claims 1 and 3 **methods of inducing analgesia in a patient** comprising administration of compounds of **formula (I) and (Ib)**, both of which encompass **loxapine**. Single dosages of these compounds for **injection**, infusion, or ingestion will generally vary from **5 to about 1,500 mg**, with a preferred dosage ranging from **7.5 to about 45 mg** per day, administered orally, with appropriate adjustment for body weight of an individual (pg. 17, lines 4-13). The properties recited in claims 11-15 are characteristic of injection administration of loxapine, as evidenced by Applicant's admission on page 13, paragraph [0041] of the instant specification. Injection administration encompasses intravenous administration.

***Ascertainment of the Difference Between Scope the Prior Art and the Claims
(MPEP §2141.012)***

Dehaven does not explicitly state that the compounds of formula (I) and (Ib), which encompass loxapine are intended for the treatment of headache. This deficiency is obviated per the teachings of Dehaven.

***Finding of Prima Facie Obviousness Rational and Motivation
(MPEP §2142-2143)***

It would have been prima facie obvious to an ordinary skilled artisan that a headache is characterized by pain. Thus, it would have been prima facie obvious at the time of the instant application to administer a known analgesic (e.g. loxapine or another compound of Dehaven's formulae I or Ib) to treat the pain associated with a headache. An ordinary skilled artisan would have had a reasonable expectation of success of treating a headache upon administration of loxapine, because analgesics are conventionally administered to treat pain, headaches are characterized by the sensation of pain, and loxapine has analgesic properties, as evidenced by the teachings of Dehaven.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

The rejection on the ground of nonstatutory obviousness-type double patenting of claims 1, 16-17, and 19 as being unpatentable over claims 7, 9, 10, 12, and 13 of U.S. Patent No. 6,716,416 (USPN '416) **is maintained** for the reasons of record set forth on pages 17-18 of the office action mailed on June 2, 2006 and because no terminal disclaimer has yet been filed by Applicants.

The provisional rejections on the ground of nonstatutory obviousness-type double patenting of claims 1 and 16-20 (claim 20, only with copending '877) as being unpatentable over (1) claims 12, 15, 16, and 18 of copending Application No. **10/633,876** (copending '876) and (2) claims 1 and 7-9 of copending Application No. 10/633,877 (copending '877) **are maintained** for the reasons of record set forth on pages 18-19 of the office action mailed on June 2, 2006 and because no terminal disclaimer has yet been filed by Applicants.

Claims 1 and 5-15 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1 and 15 of copending Application No. 10/719,763 (copending '763). Although the conflicting claims are not

identical, they are not patentably distinct from each other because the claims are substantially overlapping in scope and/or mutually obvious. Independent claim 1 of the instant application claims a method of treating headache by the administration of loxapine or a salt or prodrug thereof. Independent claim 1 of copending '763 claims a method of treating a headache comprising the inhalation administration of a composition comprising an antipsychotic to a patient in need of headache relief. Dependent claim 15 of copending '763 identifies suitable antipsychotics for treating headache, including, loxapine. The claims of copending '763 do not mention any specific dosages, however, it is well within the capability of the ordinary skilled artisan to determine a therapeutically effective dose of a given drug, and thus, this deficiency is considered an obvious modification. Regarding the properties recited in claims 13-15 of the instant application, these are considered to result necessarily from the inhalation administration of loxapine. Therefore, upon the inhalation administration of loxapine, such as is claimed in claim 15 of copending '763, the properties claimed in claims 13-15 of the instant application would result.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1 and 5-15 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1 and 15 of copending Application No. 11/346,548 (copending '548). Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims are substantially overlapping in scope and/or mutually obvious. Independent claim 1 of the instant application

has been described above. Independent claim 1 of copending '548 claims a method of treating headache by the administration of an antipsychotic and dependent claim 15 specifies that suitable antipsychotics for the treatment of headache include loxapine. . The claims of copending '548 do not mention any specific dosages, however, it is well within the capability of the ordinary skilled artisan to determine a therapeutically effective dose of a given drug, and thus, this deficiency is considered an obvious modification. Regarding the properties recited in claims 13-15 of the instant application, these are considered to result necessarily from the inhalation administration of loxapine. Therefore, upon the inhalation administration of loxapine, such as is claimed in claim 15 of copending '763, the properties claimed in claims 13-15 of the instant application would result.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Other Matter

The Examiner kindly thanks Applicants for pointing out the typographical error in the provisional rejection on the ground of nonstatutory obviousness-type double patenting of claims 1 and 16-20 (claim 20, only with copending '877) as being unpatentable over (1) claims 12, 15, 16, and 18 of copending Application No. 10/653,876 (copending '876). As Applicants correctly stated, the correct number of the copending application is 10/633,876 not 10/653,876.

Conclusion

Claims 1-20 and 24 are rejected. No claims are allowed.

Application/Control Number:
10/719,540
Art Unit: 1616


Page 13

Any inquiry concerning this communication or earlier communications from the examiner should be directed to James H. Alstrum-Acevedo whose telephone number is (571) 272-5548. The examiner can normally be reached on M-F, 9:00-6:30, with every other Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann Richter can be reached on (571) 272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

James H. Alstrum-Acevedo
Patent Examiner
Technology Center 1600


SABHA QAZI, PH.D
PRIMARY EXAMINER

Sabiha Qazi
Primary Patent Examiner
Technology Center 1600